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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/611,531
Filing Date: June 30, 2003
Appellant(s): VENKATRAMAN ET AL.

Philip S Yip
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 15, 2007 appealing from the Office action mailed January 12, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The amendment after final rejection filed on December 19, 2006 has been entered.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

Appealed claims are 12-33, 54-57, 59-60.

(8) Evidence Relied Upon

US 4,638,043	SZYCHER ET AL.	1-1987
US 5,273,757	JAEGER ET AL.	12-1993
US 6,139,866	CHONO et al.	10-2000
US 5,066,648	ALEXANDER ET AL.	11-1991
US 5,599,289	CASTELLANA	2-1997

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

(A) Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 12, 13, 15-20, 22, 33, and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by 4,638,043 ('043).

US '043 discloses a transdermal drug releasing patch that is non-toxic, non-carcinogenic and biocompatible, oxygen and water vapor permeable, flexible, and can incorporate a wide variety of drugs for a controlled, sustained release to the wearer (abstract; col.2, lines 56-57). The patch comprises support layer, i.e. backing layer (12); a polymer layer of polyurethane containing a drug (16) and a pressure sensitive adhesive layer to fix the patch to the skin (18), i.e. maintaining the patch in drug transmitting relationship with the body surface (col.2, lines 13-22; col.4, lines 45-57; figures 2 and 3). The drug is contained in an amount of 1-10% in the polyurethane layer and includes analgesics (col.2, line 31; col.3, lines 59-60). The drug and a material that aids in the transport of the drug into the skin, i.e. permeation enhancer, are blended into the polyurethane layer (col.4, lines 1-7). The drug containing layer is made of polyurethane comprises the reaction product of dicyclohexyl methane diisocyanate, polytetramethylene ether polyol, and 1,4-butane diol which is TECOFLEX^{R} (col.8, lines 56-65). The polyurethane polymer is liquid at room temperature to facilitate admixture of drug to form a homogenous blend, and this implies that the melt temperature of the polyurethane is below 100^{0} C and the drug can be blended into the polymer at this temperature (col.2, lines 42-46). The polyurethane polymer does not contain any solvents (col.3, lines 32-33). The modulus of the melt-blended mixture claimed in claim 33 is inherent to specific polymer and specific drug.

(B) Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

i) Claims 12-20, 22, 33, 54 and 59-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,638,043 ('043).

US '043 teaches a transdermal drug releasing patch that is non-toxic, non-carcinogenic and biocompatible, oxygen and water vapor permeable, flexible, and can incorporate a wide variety of drugs for a controlled, sustained release to the wearer (abstract; col.2, lines 56-57). The patch comprises support layer, i.e. backing layer (12); a polymer layer of polyurethane containing a drug (16) and a pressure sensitive adhesive layer to fix the patch to the skin (18), i.e. maintaining the patch in drug

transmitting relationship with the body surface (col.2, lines 13-22; col.4, lines 45-57; figures 2 and 3). The drug is contained in an amount of 1-10% in the polyurethane layer and includes analgesics (col.2, line 31; col.3, lines 59-60). The drug and a material that aids in the transport of the drug into the skin, i.e. permeation enhancer, are blended into the polyurethane layer (col.4, lines 1-7). The drug containing layer is made of polyurethane comprises the reaction product of dicyclohexyl methane diisocyanate, polytetramethylene ether polyol, and 1,4-butane diol (col.8, lines 56-65). The polyurethane polymer is liquid at room temperature to facilitate admixture of drug to form a homogenous blend, i.e. below 100^0 C (col.2, lines 42-46). The polyurethane polymer does not contain any solvents that may hinder the effectiveness of many drugs (col.3, lines 32-33).

However, US '043 does not explicitly teach that the process temperature and the modulus of the polyurethane polymer. The process temperature and the modulus of the polyurethane polymer disclosed by US '043 are expected to be the same as instantly claimed because the reference teaches the same polymer formed from the same polymer reaction that is liquid at room temperature, i.e. below 100^0 C but does not specify temperature between 40^0 C and 90^0 C.

The temperature between 40^0 C and 90^0 C does not impart patentability to the claims absent evidence to the contrary.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery patch comprising a polyurethane polymer layer containing a drug wherein the polyurethane layer is liquid at

room temperature and contains no solvents as disclosed by US '043, and adjust the temperature to that required to melt the drug into the liquid polyurethane polymer according to specific drug used without the use of any solvents, motivated by the teaching of US '043 that the absence of solvent is advantageous because solvents hinder the effectiveness of many drugs, with reasonable expectation of having transdermal drug delivery patch containing polyurethane polymer layer that is non-toxic and biocompatible produced without using any solvents at a temperature below 100^0 C, thus, reserving the drug effectiveness and providing the maximum desired effect to the patient.

ii) Claims 12-33, 54-57, 59-60 rejected under 35 U.S.C. 103(a) as being unpatentable over US '043 in view of US 5,273,757 ('757) or *vise versa*.

The teachings of US '043 are discussed above. US '043 does explicitly teach that the process temperature and the modulus of the polyurethane polymer. US '043 does not teach specific drugs and permeation enhancer and the amounts of all the ingredients. US '043 does not teach the acrylate adhesive in skin contact layer.

The specific drugs and enhancers as well as amounts of different ingredients do not impart patentability to the claims, absent evidence to the contrary.

The acrylate adhesive is known as skin contact layer, its instant use does not impart patentability to the claims, absent evidence to the contrary.

US '757 teaches transdermal drug delivery device suitable to deliver drug to the skin comprises backing layer, and hot melt adhesive layer comprising 10-100%

polyurethane adhesive, 10-80% plasticizer such as fatty acid esters, and drug such as fentanyl (abstract; col.col.3, lines 25-30, 54; col.4, lines 6-9, 39-43). The hot melt adhesive layer has process temperature between 40^0 C and 80^0 C and does not contain any solvent therefore the process is advantageous manner for less temperature-sensitive substances because no toxic solvent residues can remain in the transdermal patch, less time consuming, less environmental polluting, and coast saving (col.2, lines 54-61; col.4, lines 43-54).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device that has matrix formed of melt blend of polyurethane, active agent and permeation enhancer as disclosed by US '043, and use a temperature process between 40^0 C and 80^0 C and fentanyl as an active agent, and fatty acid ester as an enhancer as disclosed by US '757, motivated by the teaching of US '757 that process temperature between 40^0 C and 80^0 C without solvent is advantageous manner for less temperature-sensitive substances because no toxic solvent residues can remain in the transdermal patch, less time consuming, less environmental polluting, and coast saving, with reasonable expectation of having transdermal drug delivery device that has matrix comprising melt blend of polyurethane, fentanyl, and fatty acid ester that is processed at 40^0 C and 80^0 C without solvent that is advantageously prepared in a manner suitable for less temperature-sensitive substances, not toxic, less time consuming, less environmental polluting, and coast saving, and meanwhile deliver fentanyl effectively in enhanced manner to the skin of the patient in need of such treatment.

Vise versa, US '757 does not teach the skin contact layer of the transdermal device or the specific starting material for the polyurethane.

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal device to deliver fentanyl comprising matrix of polyurethane having a process temperature between 40^0 C and 80^0 C without solvent as disclosed by US '757, and add the skin contact layer to protect the matrix as disclosed by US '043, and replace the polyurethane by the polyurethane produced by the reaction product of dicyclohexyl methane diisocyanate, polytetramethylene ether polyol, and 1,4-butane diol as disclosed by US '043, motivated by the teaching of US '043 that such polyurethane is non-toxic, non-carcinogenic and biocompatible, oxygen and water vapor permeable, flexible, and provides a controlled, sustained release of the drug to the wearer, with reasonable expectation of having a matrix comprising fentanyl, fatty acid enhancer, and polyurethane produces by the reaction product of dicyclohexyl methane diisocyanate, polytetramethylene ether polyol, and 1,4-butane diol that is non-toxic, non-carcinogenic and biocompatible, oxygen and water vapor permeable and flexible that provides controlled, sustained release of fentanyl to the wearer.

iii) Claims 21, 28, 29 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '043 in view of US '757 and further in view of US '6,139,866 ('866).

The combined teachings of US '043 and US '757 are discussed above.

The combination of US '043 with any of US '757 does not specifically teach the glycerol monolaurate permeation enhancer, or acrylate adhesive as skin contact layer.

US '866 teaches percutaneous formulation to deliver fentanyl wherein the formulation is stable and has little irritation to the skin and excellent in percutaneous permeation of fentanyl (abstract). The formulation comprises 0.05-20% of fentanyl, 0.1-98% of pressure sensitive adhesive that can be acrylate adhesive, and 0.01-20% of permeation enhancer such as glycerol monolaurate which has recognized absorption enhancing effect on the skin (col.1, lines 65-67; col.2, lines 1-2, 67; col.4, lines 9-11, 28-31, 37-39).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device that has matrix formed of melt blend of polyurethane, fentanyl and fatty acid permeation enhancer as disclosed by US '043 combined with US '757, and replace the permeation enhancer by glycerol monolaurate and further use acrylate as skin contact adhesive as disclosed by US '866, motivated by the teaching of US '866 such a percutaneous formulation comprising glycerol monolaurate and acrylate adhesive delivers fentanyl with little irritation to the skin and provides excellent recognized percutaneous permeation, with reasonable expectation of having a transdermal melt blend matrix comprising polyurethane, fentanyl and glycerol monolaurate and acrylate skin contact layer wherein the device has excellent permeation to fentanyl without skin irritation.

iv) Claims 21, 28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '043 in view of US '757, and further in view of US 5,066,648 ('648).

The combined teachings of US '043 and US '757 are discussed above.

The combination of US '043 with US '757 does not specifically teach lauryl pyroglutamate as a permeation enhancer.

US '648 teaches pryoglutamic acid esters as safe dermal permeation enhancers being capable of improving delivery of active agent through the skin and into the general circulation and undergo fast metabolic breakdown into non-toxic metabolic products as soon as they reach the live area of the skin (abstract; col.3, lines 25-42).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device that has matrix comprising melt blend of polyurethane, fentanyl and permeation enhancer as disclosed by US '043 in combination with US '757, and replace the enhancer by pyroglutamic acid esters as disclosed by US '648, motivated by the teaching of US '648 that pryoglutamic acid esters are safe dermal permeation enhancers capable of improving delivery of active agent through the skin and into the general circulation and undergo fast metabolic breakdown into non-toxic metabolic products as soon as they reach the live area of the skin, with reasonable expectation of having a transdermal device that deliver fentanyl from a melt blend matrix comprising polyurethane and lauryl pyroglutamate with improved permeation of fentanyl to the circulation without causing any toxic effects.

v) Claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over US '043 in view of US '757, and further in view of US 5,599,289 ('289).

The combined teachings of US '043 and US '757 are discussed above.

The combination of US '043 with any of US '757 does not specifically teach the skin contact adhesive as acrylate adhesive.

US '289 teaches wound dressing comprising skin contact acrylate adhesive layer that is preferred because it is hypoallergenic and non-irritating to the skin (col.5, lines 35-39, 45-49).

Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal drug delivery device that has matrix formed of melt blend of polyurethane and fentanyl, and skin contact layer as disclosed by US '043 in combination with US '757, and use acrylate adhesive to form the skin contact layer as disclosed by US '289, motivated by the teaching of US '289 that acrylate adhesive layer is preferred because it is hypoallergenic and non-irritating to the skin, with reasonable expectation of having transdermal drug delivery device that has matrix formed of melt blend of polyurethane and fentanyl, and comprising an acrylate adhesive skin contact layer that can be worn by the patient without causing irritation or allergic reaction, thus, delivers the active agent comfortably to the user.

(10) Response to Argument

Regarding 35 USC § 102(b):

Appellant argue that claims 12, 13, 15-20, 22, 23, and 54 are not anticipated by US 4,638,047 ('047 Szycher)

Claims 12, 13

Appellants argue that Szycher described only UNCURED material and never mentioned that the cured material can be mixed or blended, or melting temperature. He never mentioned that the polyurethane layer is liquid at room temperature, only that the precured oligomeric material is liquid. The liquid PRECURED polymeric liquid is not yet cured and therefore is not polyurethane. Szycher stated clearly that the drug dispensing member is comprised of "a polyurethane formed from an oligomer which is cured by actinic radiation", the drug is incorporated in the material before the material is cured (Column 4, lines 10-14). Curing changes the thermal and mechanical property of a material, because of cross-linking formed in the curing reaction.

(1) The process temperature is not inherent

The term "melt-blend" or "melt mix" indicates, melting is involved. Melting thermoplastic polymer and blending in the drug are also described in described in US 6010715. Thus, it is clear that to those skilled in the art that melt blending in the present invention involves raising the temperature to melt the polyurethane from a unmelted state and mixing in the drug. Szycher never mentioned melt blending. Appellants submit that Szycher disclosed precured liquid material that cannot be melt-blended, since it being already a liquid cannot be processed by melting. Szycher might have mentioned

raising temperature to cause the curing of oligomers, but such curing temperature is certainly not the "processing temperature" in which the polyurethane material is heated to melt in melt-blending.

(2) Mixing of drug in polyurethane before or after Curing imparts patentability

Appellant argue that the melt mixing of the drug in polyurethane without the need for curing does impart patentability to the product claims. Whether something is cured or not has great impact on the property of a device and thus impact patentability. By requiring curing, the referenced Szycher material has property vastly different from material that can be melt blended, and therefore cannot be used for anticipating the present invention. The precured oligomer material cannot be melt-blended because it cannot melt.

(3) The end products are materially different before and after curing

The end product is materially different from the end product of Szycher because the present end product includes mixture including polyurethane that has a process temperature of less than about 150 °C, at which melt blending can be done. There is absolutely no evidence that the Szycher cured end product has polyurethane that has such property.

(4) Szycher did not show TECOFLEX can be used for drug-containing layer

Appellant argue that Szycher DID NOT "disclosed that the materials used to make the

drug containing layers is the same as the materials used to make the substrate but without the drug". Rather, Szycher merely said that "the polyurethane formed in the drug release system" is also suitable for the substrate layer. Even assuming Szycher did suggest TECOFLEX could be used in the drug-containing layer, that still does not mean Szycher suggested TECOFLEX of the kind having processing temperature of less than about 150 °C was to be used., or that it could be used without curing

Certain claims are separately patentable and further different from Szycher

Appellant argue that other than claims 13-14 which are related to process temperatures, the other claims under appeal do not stand and fall with claim 12, and are patentable separately. The reason is that the monomeric composition of the polyurethane, the permeation enhancers, and specific drug were mentioned and these would affect the process temperature of the mixture and the amount of the drug as delivered, as well as the adhesive property of the resulting material. Something that can be used in one System does not mean it will be applicable in a different system. Claim 15 to 19 mention specifics about the polyurethane. Claims 20-32, 57, and 59 include specific ranges of drug, permeation enhancer, or polyurethane in the drug reservoir. Claims 27-32, 57, and 59 especially stated the amount of polyurethane polymer in the drug reservoir. Claims 31-32 address having an in-line adhesive. Claim 33 addresses the mixture having a particular modulus. Claims 54-56 mentions not having phase separation. These claims are not anticipated by Szycher.

Appellants arguments filed 03/15/2007 against 102 rejection have been fully considered but they are not persuasive.

Appellants' attention is drawn to the scope of the present claims that are directed to product by process to produce transdermal drug delivery device containing drug-containing layer consisting of polyurethane that processed at temperature less than 150^0 C. It has been held that product by process claims are not limited to the manipulation of the predicted steps, only the structure implied by this steps. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Szycher disclosed transdermal drug delivery system comprising a layer of polyurethane comprising a drug. The reference disclosed mixing at room temperature, and the claims included in the rejection recite temperature less than 150 ^{0}C (claim 12) or less than 100 ^{0}C (claim 13). The room temperature is known in the art between to be between 20 ^{0}C and 35 ^{0}C. Therefore, the claimed process temperature of polyurethane is disclosed by the prior art. The product disclosed by the Szycher is identical to the claimed product and both products are not materially different from each other. Mixing the drug in the polyurethane layer before or after the curing is directed to method steps for the production of the device, and therefore does not impart patentability to the claims

directed to product. The burden is on applicants to show that blending the polymer with the drug after curing the polymer will provide a product materially different from the blending the polymer with the drug before curing. The reference disclosed the polyurethane made from the same elements as instantly claimed. It has been held that when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product claimed in a product-by-process claim, a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtains prior art products and make physical comparisons therewith. *In re Brown,* 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972). It has been held that once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi,* 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir.1983). The Board further stated *In re Ex parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989) that applicant should make some comparison between factors affecting the production of the product to establish unexpected properties since the materials appeared to be identical or only slightly different. That applies on the present case regarding mixing before curing or after curing.

Regarding appellants argument against TECOFLEX, it is interpreted by the examiner that same material can be used effectively in both drug containing layer and substrate or materials for both layers can be used interchangeably. In any event, the drug containing layer is disclosed by Szycher to be made of polyurethane that made from the same starting materials as instantly claimed.

Regarding appellants argument that claims 14-19, 20-32, 57 and 59 are separately patentable and different from Szycher, it is noted that these claims are not included in the anticipatory rejection. Appellants further argue, claims 54-57 mention not having phase separation, and not anticipated by Szycher. It is noted that Szycher does not mention phase separation either, therefore, claim 54 is anticipated by Szycher. Claims 55-57 are not included in the anticipatory rejection.

Regarding 35 USC § 103(a):

Appellant argue that claims 12-20, 22, 33, 54 and 57-60 are not patentable over US 4,638,047 ('047 Szycher)

Claims 13, 14

Appellant hereby repeat the argument against Szycher.

Appellants further argue that:

Certain claims are separately patentable and further different from Szycher

Applicant argue that other claims under appeal do not stand and fall with claim 12. The reason is that the monomeric composition of the polyurethane, the permeation

enhancers, and the specific drug affect the process temperature of the mixture and the amount of the drug as delivered, as well as the adhesive property of the resulting material. Claim 15 to 19 mention specifics about the polyurethane. Claims 20-32, 57, and 59 include specific ranges of drug, permeation enhancer, or polyurethane in the drug reservoir. Claims 27-32, 57, and 59 especially stated the amount of polyurethane polymer in the drug reservoir. Claims 31-32 address having an in-line adhesive. Claim 33 addresses the mixture having a particular modulus. Claims 54-56 mentions not having phase separation. These claims are neither anticipated or rendered obvious by Szycher.

The examiner is hereby repeats the same response regarding Szycher reference as set forth in this Examiner's Answers.

In response to argument regarding claims separately patentable, it is argued that claim 12 is obvious over Szycher, and therefore claims 13-20, 22, 23, and 59-60 that depends on claim 12 are not patentable.

The specific temperature and amounts of ingredients, as well as the specifics about polyurethane, all do not impart patentability to the claims, absent evidence to the contrary. The references do not specifically teach adding the ingredients in the amounts claimed by applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan

of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention.

It is noted that claims 27-33, 57 and are not included in the rejection.

It is noted that Szycher does not mention phase separation, therefore, claim 54 is obvious over Szycher.

Appellant argue that claims 12-33, and 54-57 and 59-60 are not patentable over US 4,638,047 ('047 Szycher) in view of US 5,273,757 ('757 Jaeger) or *vise versa*

Claims 13, 14

Appellants hereby repeat the argument regarding Szycher, and argue that Jaeger does not cure the shortcomings of Szycher. Appellants argue that Jaeger teaches that the pressure sensitive adhesive can contain only up to 10 to 50% by weight of polyurethane, and the adhesive composition contains a lot of other material, such as hydrogenated alcohol, hydrocarbon resin, esters of vegetable fatty acids, and fillers. Much of these other ingredients were soft materials and perhaps liquid, including a large amount of plasticizers. There may be as low as 10% polyurethane polymer with as much as 40% vegetable fatty acids ester plasticizer. Polyurethane was only one of many scores of alternative polymers listed. It is a scientific fact that plasticizers are able to decrease the glass transition temperature and the melt viscosity of a hot melt

polymer. Jaeger stated that the pressure sensitive adhesive mixture with drug active substance as well as other excipients has a processing temperature of 40-80 °C. But Jaeger did not say that the polyurethane of the adhesive has a processing temperature of 40-80 °C. There is no expectation of success that polyurethane without a large amount of plasticizer can be processed at that temperature range. If a person were to combine Szycher with Jaeger, the result would be cured polyurethane with lots of plasticizers. Such combinations would not result in the claimed product of the present application. It is not obvious at all that the polyurethane with processing temperature of less than 150°C is present in the adhesive in Jaeger or that Jaeger could produce uniform hot melt drug-containing layer from polyurethane.

Appellant further argue that :

Other claims patentable separately

Regarding claims other than claim 12, and 13-14 which are related to process temperatures, the other claims under appeal do not stand and fall with claim 12. The reason is that the monomeric composition of the polyurethane, the permeation enhancers, and the specific drag affect the process temperature of the mixture and the amount of the drug as delivered. In particular, claim 15 to 19 mention specifics about the polyurethane. Claims 20-32, 57, and 59 include specific ranges of drug, permeation enhancer, or polyurethane in the drug reservoir. These ranges are generally outside the ranges of what Jaeger disclosed. Claims 27-32, 57, and 59 especially stated the amount of polyurethane polymer in the drug reservoir and the ranges are substantially

more than that disclosed by Jaeger. Claims 31-32 address having an in-line adhesive. Claim 33 addresses the mixture having a particular modulus. Claims. 54-56 mentions not having phase separation. No combination of Szycher and Jaeger Would render these claims obvious.

In response to the argument regarding Szycher's reference, examiner's response set forth in this office action is hereby repeated.

Appellants' attention is drawn to the scope of the present claims that are directed to transdermal drug delivery device, and the drug-containing layer consisting of polyurethane that has process temperature less than 150^0 C. Szycher disclosed transdermal drug delivery system comprising a layer of polyurethane comprising a drug processed at room temperature, i.e. temperature below 100^0 C. Jaeger disclosed transdermal drug delivery device comprising adhesive layer comprising polyurethane, and suggested adhesive polymer forming 10-100% of the adhesive composition, col.5, line 36; therefore the reference suggested adhesive composition that can has 100% adhesive polymer. With careful review to col.6, lines 13-21 of Jaeger's reference where polyurethane adhesive composition was disclosed, it is noticed that the adhesive composition as a whole contains 10-50% polyurethane, however, no other adhesive polymers are included in the composition, therefore, polyurethane is the only adhesive polymer forming 100% of the adhesive polymer. In other words, the polymer consisting of polyurethane.

The claims' language using the expression "comprising" in terms of the composition of the drug reservoir as a whole, and this expression does not exclude other ingredients, active or inactive, even in major amounts. The present claims recite permeation enhancers which are also fatty materials encompassed by the plasticizers and excipients disclosed by Jaeger's reference.

The disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

Regarding the process temperature, the examiner's response regarding product by process as set forth in this office action is hereby repeated the process temperature is directed to the method of making steps, and not part of the product limitation. In any event, Jaeger recognized making the adhesive layer containing the polymer and drug by melting the adhesive and the drug at a temperature that is safe and advantageous to heat sensitive drugs that ranges from 40^0 C and 80^0 C.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., adhesive of Jaeger could produce uniform hot melt) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims do not recite uniform hot melt.

Regarding appellants argument that no expectation of success and if the references were combined the present invention will not be obvious, the examiner

recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Jaeger recognized making the adhesive layer containing the drug by melting the adhesive and the drug at a temperature that is safe and advantageous to heat sensitive drugs that ranges from 40^0 C and 80^0 C. One having ordinary skill in the art at the time of the invention would have benefit from the teaching of Jaeger to melt the adhesive and the other ingredient without solvent using the minimal suitable temperature because this process is advantageous manner for temperature-sensitive substances, and no toxic solvent residues can remain in the transdermal patch, less time consuming, less environmental polluting, and coast saving.

In considering the disclosure of the reference, it is proper to take into account not only the specific teachings of the reference but also the inferences which one skilled in the art would reasonably be expected to draw therefrom. *In re Preda*, 401 F.2d 825, 826, 159 USPQ 342, 344 (CCPA 1968). The rational to modify or to combine the prior art does not have to be expressly stated in the prior art; the rational may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art. The reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve different problem. It is not necessary that the prior art suggest the combination

or modification to achieve the same advantage or result discovered by applicant. *In re Linter*, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972).

It is well established that the claims are given the broadest interpretation during examination. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969).

In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been *prima facie* obvious within the meaning of 35 U.S.C. 103 (a).

Regarding appellants argument that other claims are patentable separately, it is argued that claim 12, 55-57 are obvious over the combined teachings of Szycher and Jaeger, and therefore dependent claims 13-33, and 54, 59-60 are not patentable.

The specific temperature and amounts of ingredients, as well as the specifics about polyurethane, all do not impart patentability to the claims, absent evidence to the contrary. The references do not specifically teach adding the ingredients in the amounts claimed by applicant. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to

best achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention.

It is noted that Szycher and Jaeger do not mention phase separation, therefore, claim 54 is obvious over the combination of Szycher and Jaeger.

Appellant argue that claims 21, 28, 29, 31 and 32 are not patentable over US 4,638,047 ('047 Szycher) combined with US 5,273,757 ('757 Jaeger) and further in view of US 6,139,866 ('866 Chono)

Claims 21, 28-29

Appellants hereby repeat the argument regarding Szycher combined wit Jaeger. Appellants further argue that Chono does not teach polyurethane and teaches the adhesive layer containing the drug is made with solvent, and this is irrelevant to the melt blending at the temperatures of the present invention.

Appellants argue that:

Other claims patentable separately

Claims 31-32 address having an in-line adhesive and therefore are separately patentable from the other claims (21,28-29) rejected under references including Chono. No combination of Szycher, Jaeger and Chono would render these claims obvious.

In response to the argument regarding combination of Szycher's and Jaeger and melt blending, the examiner's response set forth in this office action is hereby repeated.

In response the argument regarding Chono, it is argued that Chono is relied upon for the solely teaching of the effective transdermal therapeutic dose of fentanyl and for teaching glycerol monolaurate as permeation enhancer for drugs. Chono is relied upon also for teaching acrylate adhesive as safe skin contact layer. Polyurethane is taught by the Szycher as well as permeation enhancers, and one having ordinary skill in the art would have been replaced the permeation enhancer taught by Szycher by glycerol monolaurate taught by Chono, and further use acrylate as skin contact adhesive as disclosed by Chono, motivated by the teaching of Chono that such a percutaneous formulation comprising glycerol monolaurate provides excellent recognized percutaneous permeation of fentanyl, and acrylate contact adhesive has little irritation to the skin and, with reasonable expectation of having a transdermal device comprising layer comprising polyurethane, fentanyl and glycerol monolaurate, and further add acrylate adhesive skin contact layer wherein the device has excellent permeation to fentanyl without skin irritation. Chono is an analogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Chono is from the field f applicants' endeavor, and one having ordinary skill in the art seeking for

permeation enhancer for fentanyl and skin contact adhesive layer would have definitely looked at Chono's disclosure that delivers fentanyl transdermally.

Appellant argue that claims 21, 28 and 30 are not patentable over US 4,638,047 ('047 Szycher) combined with US 5,273,757 ('757 Jaeger) and further in view of US 5,066,648('648 Alexander)

Claims 21, 28 and 30

Appellants hereby repeat the argument regarding Szycher combined wit Jaeger. Appellants argue that anybody skilled in the art knows that permeation enhancers do not function the same way for different drugs in different matrixes. Alexander does not mention fentanyl, and does not mention polyurethane as the drug layer carrier polymer or melt-blending.

In response to the argument regarding combination of Szycher's and Jaeger and melt blending, the examiner's response set forth in this office action is hereby repeated.

In response to this argument, it is argued that Alexander teaches that pryoglutamic acid esters are useful to deliver analgesics and sedatives (col.5, lines 52, 56). The reference teaches that pryoglutamic acid esters enhance skin permeation of the therapeutic agent (col.4, lines 45-46). Hence permeation enhancers do not react with the drug or the matrix materials. Enhancers act as skin softener to soften the stratum corneum of the skin that acts as a barrier. The amount of the enhancers used is

the parameters that is affected by the kind of the drug and the adhesive, and not enhancer itself. Pryoglutamic acid esters will enhance the delivery of any drug and its amount depends on the solubility, hydrophilicity and lipophilicity of the drug that control the transport of the drug across the stratum corneum.

Appellant argue that claim 32 is not patentable over US 4,638,047 ('047 Szycher) combined with US 5,273,757 ('757 Jaeger) and further in view of US 5,955,289 ('289 Castellana)

Appellants hereby repeat the argument regarding Szycher combined wit Jaeger. Appellants further argue that Castellana teaches wound dressing comprising skin one layer of acrylate adhesive and does not teach polyurethane layer made by melt blending, therefore one would not make the presently claimed invention from the teaching of Castellana.

In response to the argument regarding combination of Szycher's and Jaeger and melt blending, the examiner's response set forth in this office action is hereby repeated.

In response, it is argued that Castellana reference is relied upon for the solely teaching of skin contact acrylate adhesive layer. It has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Castellana is

from the field f applicants' endeavor, and one having ordinary skill in the art would have used acrylate adhesive in the skin contact layer of transdermal device motivated by the teaching of Castellana that acrylate adhesive layer is preferred because it is hypoallergenic and non-irritating to the skin, with reasonable expectation of having transdermal drug delivery device that has matrix formed of melt blend of polyurethane and fentanyl, and comprising an acrylate adhesive skin contact layer that can be worn by the patient without causing irritation or allergic reaction, thus, delivers the active agent comfortably to the user.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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